

**REMARKS**

Claims 39, 57 and 70 have been amended. Support for these amendments can be found, for example, on page 9 and in the examples in the specification.

Claims 40, 41, 58, 59, 71 and 72 have been canceled.

Upon entry of the Amendment, claims 39, 42-57, 60-70 and 73-90 will be pending.

The abstract of disclosure is objected to for not appearing on a separate sheet of paper.

Applicants provide herewith the abstract on a separate sheet of paper. The Examiner has indicated that the content of the abstract is acceptable. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the objection.

Claims 39-48, 52-82 and 89 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Porssa et al., U.S. Patent No. 6,251,964 (“Porssa”).

Claim 39 has been rejected over Porssa. The Examiner asserts that the identical polymer is used to coat a stent in Porssa in the same process steps so that the resulting coating would inherently have the same dry thickness.

Applicants traverse the rejection.

Applicants submit that the coating process significantly affects the thickness of the polymer coating deposited. For instance, in Example 6 of Porssa, the polymer coating solution was 10 mg/ml. In the present examples, such as Example 1.1, the polymer solution had a concentration of 50 mg/ml. In Example 1:2, further tests are done using this polymer solution, with higher coating weights. In Example 1:2, it is concluded that the uptake of drug in the case of the cationic polymer is related to polymer volume not just surface area. Thus, the results

show that the greater the thickness of polymer, which is the higher the volume of coating solution used to coat the surface, the higher the level of drug taken up. By comparing the examples in Porssa with the examples of the present invention, it is evident that the selection of the minimum thickness, as in claim 1, for the polymer is technically significant and provides a beneficial effect in terms of the drug loading level which can be achieved.

There is nothing in Porssa that discloses or suggests that the selection of any particular thickness for the polymer coating provides a different potential loading level with anionic active. Therefore, Porssa does not anticipate claim 39 of the present invention.

Claims 40-48 and 52-56 depend directly or indirectly from claim 39. Therefore, claims 40-48 and 52-56 are not be anticipated by Porssa at least by virtue of their dependency on claim 39.

The Examiner also asserts that claims 57 and 70 are anticipated by Porssa. However the Examiner has overlooked the features in those claims defining the pharmaceutical active. In claim 57, the active is a nucleic acid whereas in claim 70 the active is a protein. There is no disclosure in Porssa of unionically charged proteins, or indeed any proteins, as pharmaceutical actives, nor of nucleic acids. Therefore, Porssa does not anticipate Applicants' claim 57 or claim 70. The Examiner acknowledges this at the end of the first paragraph on page 5 of the Office Action.

Claims 58-69 and 89 depend directly or indirectly from claim 57 and claims 71-82 depend directly or indirectly from claim 70. Thus, these claims are not be anticipated by Porssa at least by virtue of their dependency on claims 57 and 70.

In view of the foregoing, Applicants respectfully request that the Examiner reconsider and withdraw the rejection.

Claims 49-76, 83-88 and 90 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Porssa et al. further in view of both WO-A-98/15575 (“WO ‘575”) and U.S. Patent No. 5,674,192 (“U.S. ‘192”).

The Examiner asserts that it would be obvious to use the actives of WO ‘575 or US ‘192 in place of the active in Porssa.

Applicants traverse the rejection.

As discussed above, there is nothing in Porssa that discloses or suggests that the selection of any particular thickness for the polymer coating provides a different potential loading level with anionic active.

Additionally, Applicants submit that one of ordinary skill in the art would not be motivated to replace the heparin (a mucopolysaccharide) in Porssa with the active of WO ‘575. WO ‘575 is strictly related to delivery of nucleic acids having particular characteristics. When Porssa discusses stents, Porssa describes release of an active into the circulation from the stent acting as a reservoir. In contrast, WO ‘575 describes delivering the nucleic acid active into the vessel wall adjacent to the stent located in the vessel. Thus in WO ‘575 a different active is being delivered to a different location. Indeed the diseases being treated in WO ‘575, namely treating vascular proliferative disorders, are very different from those diseases potentially treated by heparin, namely to reduce thrombosis. Accordingly there is no motivation to use the active of WO ‘575 to replace the active of Porssa.

Moreover, U.S. '192 describes delivery of drugs from hydrogel coatings on balloons, which result in the active being squeezed, as from a sponge, into the vessel wall. The Examiner asserts that U.S. '192 discloses delivery of actives from a hydrogel coating of a stent. A stent is mentioned in Figures 4 to 6 and from column 10, line 32 onwards. "The drug is delivered to adjacent tissue upon initial compression of the polymer and thereafter a slow sustained time release of drug remaining in the hydrogel polymer occurs (column 10 lines 58 to 63). It is clear that the drug should be delivered into the wall of the vessel, as set forth from column 8, line 40 to 43. Further at lines 47 to 50, the release of active into body fluids downstream of the treatment area is to be avoided. This is in complete contrast to Porssa, where the objective of using a stent as a reservoir for drug is that drug is released into the circulation over a period of time. It is not required in Porssa that the drug be delivered into the vessel wall adjacent to the site of implantation. Thus it would not have been obvious to one of ordinary skill in the art to replace heparin in Porssa with one of the protein or nucleic acid actives mentioned in US '192, in view of the different target for the drugs.

Since a person skilled in the art would not be motivated to replace the drugs of Porssa by one of the drugs of U.S. '192, or the nucleic acid of WO '575, the claimed invention would not be obvious based on the combination of Porssa, WO '575 and U.S. '192.

Furthermore, the Examiner accepts that Porssa does not disclose the thickness required in claim 39. Although U.S. '192 mentions thicknesses for the hydrogel coatings, these are not the same polymers as in the claims of the present application. Moreover, there is no disclosure that these thicknesses would be applicable to the polymer coatings of Porssa (or of the present invention).

This is an additional reason as to why the claimed invention, particularly the invention claimed in Applicants' claim 39 and the claims depending therefrom, would not be obvious over the combination of Porssa in view of U.S. '192 and WO '575.

WO '575 does not disclose stents coated with polymers. Balloon catheters coated with polymers are disclosed at page 20, line 4. Stents are disclosed at page 15, lines 8 to 10, but as causes of arterial injury, not as part of the solution of the invention. Thus, there is no disclosure to use stents as delivery devices for the nucleic acids of WO '575. This is yet another reason why it would not have been obvious to one of ordinary skill in the art that the nucleic acid of WO '575 could be delivered from the stent device of Porssa.

In view of the foregoing, Applicants submit that the claimed invention would not be obvious over Porssa in view of WO '575 and U.S. '192. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 39-90 have been provisionally rejected on the ground of non-statutory obviousness-type double patenting, as allegedly being unpatentable over claims 1-84 of co-pending U.S. Application No. 10/842,416 in view of WO '575 and U.S. '192.

Applicants traverse the rejection.

Applicants submit that the present claims are patentably distinct from claims 1-84 of co-pending U.S. Application No. 10/842,416. The present claims are directed to the combination of a polymer having cationic groups as well as zwitterionic groups, and an anionic active. There is no disclosure in U.S. Application No. 10/842,416 regarding this combination. In fact, the working examples in U.S. Application No. 10/842,416 disclose zwitterionic polymers which have no cationic moiety. The polymer is, for instance the same as one of the reference polymers

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used in Example 1 of the present invention. The present examples show that there is a particular benefit in using the cationic polymer in combination with anionic actives, which would not be expected from U.S. Application No. 10/842,416. For instance note the data in Table 1 on page 13 of the present specification, which shows that the presence of a cationic group, i.e. in polymer types 2.1 and 2.2, gives high loadings of the nucleic acid. The loading may be increased by increasing the thickness of the polymer coating, as shown in Table 2. These results are repeated with another nucleic acid in example 2, and plasmid DNA in example 3. In example 9, the results can be seen to be applicable to an antibody (protein),

In view of the foregoing, it is clear that the difference between the claims of the present invention and claims 1-84 of U.S. Application No. 10/842,416 is in the type of polymer and the type of active. Even if it were obvious to replace the active of U.S. Application No. 10/842,416 with the nucleic acid of WO '575, the method of the present invention would not be achieved since the polymer characteristics are not disclosed in U.S. Application No. 10/842,416. The present examples show there is a unexpectedly superior benefit in using the combination of cationic polymer and anionic active which would not be expected from U.S. Application No. 10/842,416. Accordingly, claims 39-90 would not be obvious over claims 1-84 of U.S. Application No. 10/842,416 in view of WO '575 and U.S. '192. Reconsideration and withdrawal of the rejection are respectfully requested.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

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The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

  
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